REMARKS

Upon entry of this amendment, claims 1, 9 and 12 will be amended, whereby claims 1-14 will remain pending, with claims 1, 2, 9 and 12 being independent claims.

The claim amendments are being made merely to clarify claim language, and the amendments are not intended to narrow the scope of the claimed invention. Accordingly, it is respectfully submitted that no estoppel should be associated therewith.

Reconsideration and allowance of the application are respectfully requested.

RESPONSE TO FORMAL MATTERS

Information Disclosure Statement

The Office Action indicates that the Information Disclosure Statement filed October 22, 2001 fails to comply with the rules, because it is asserted that it does not include a concise explanation of the relevance, as it is presently understood by the individual most knowledgeable about the content of the information, of each patent listed that is not in the English language. The Office Action indicates that the disclosure statement has been placed in the file, but the information referred to therein has not been considered.

In response, Applicants note that the document cited in the Information Disclosure Statement, i.e., WO98/46777, includes an English abstract and is cited and discussed in the specification beginning at the bottom of page 1 through the top of page 2. This English abstract and the discussion the specification comprises a concise explanation of the relevance, as it is presently understood, of this document. Accordingly, the Examiner is respectfully requested to initial the Form PTO-1449

submitted with the Information Disclosure Statement, and to forward a copy of the initialed form with the next communication from the Patent and Trademark Office. For the Examiner's convenience another copy of the form is enclosed.

Abstract Of The Disclosure

The Abstract of the Disclosure is objected to as being greater than 150 words in length.

In response, Applicants have amended the Abstract of the Disclosure to reduce to length to less than 150 words, and to remove terms such as "said". Accordingly, this ground of rejection should be withdrawn.

Drawings

Applicants note that the Office Action does not include a Form PTO-948 - Notice of Draftsperson's Patent Drawing Review attached thereto, or any comment regarding the drawings as filed. In the absence of any indication to the contrary by the Patent and Trademark Office, Applicants assume that the drawings submitted with the application are acceptable, and that no further action is required with respect to submission of formal drawings.

RESPONSE TO MAINTAINING OF RESTRICTION REQUIREMENT

The Office Action has maintained the Restriction Requirement, acknowledging Applicants' election with traverse of Group I and a membrane-bound enzyme, and has made the restriction

requirement final apparently holding claims 9-14 to be withdrawn from consideration as being directed to non-elected inventions.

The Office Action contends that membrane-bound enzyme is not directed to a species, and that each of the proteins listed in the claims are also patentably distinct inventions. However, Applicants respectfully submit that each of the proteins should be considered to be a species which are rejoindable upon allowance of the elected invention.

Applicants once again respectfully submit that for the previously submitted reasons, the restriction requirement should be reconsidered and withdrawn. In any event, whether or not the requirement is withdrawn, upon allowance of the elected claims, the Examiner is respectfully requested to rejoin the non-elected claims and species with the allowed elected claims.

In view of the above, reconsideration and withdrawal of the restriction requirement or rejoinder of the non-elected invention are respectfully requested.

RESPONSE TO REJECTIONS BASED UPON PRIOR ART

Claims 1-8 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Bandman et al. (hereinafter "Bandman"), U.S. Patent No. 5,858,750. In this ground of rejection, it is asserted, pointing to claim 8 and column 1, lines 53-56, and column 14, lines 6-12 and 29-30, that Bandman teaches a method of producing a membrane enzyme, human retinol dehydrogenase type II homolog (HRoDH), by culturing a host cell (insect cell baculovirus system) and recovering the enzyme from the host cell culture.

Moreover, claims 1-8 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Ikeda et al. (hereinafter "Ikeda"), PNAS, 1995; 92: 126-130. In this ground of rejection, it is asserted, pointing to pages 126-127, that Ikeda teaches a method of expressing and purifying a membrane-bound enzyme, human γ-glutamyl transpeptidase mutant, by recovering recombinant baculovirus from insect cells.

In response, Applicants respectfully submit that independent claim 1 is directed to a method for expressing a protein selected from a membrane-bound enzyme, a substrate of the membrane-bound enzyme, a membrane-bound enzyme activator, a membrane-bound transport protein, a channel protein, a membrane structural protein, a protein involved in adhesion, a protein involved in antigen presentation, or a protein involved in formation of high dimensional structure of a protein by culturing a host infected with at least one recombinant baculovirus which contains a gene encoding said protein, wherein said protein is expressed in a budded baculovirus released from said host.

Moreover, independent claim 2 is directed to a method for preparing a protein which comprises culturing a host infected with a recombinant baculovirus which contains a gene encoding a protein selected from a membrane-bound enzyme, a substrate of the membrane-bound enzyme, a membrane-bound enzyme activator, a membrane-bound transport protein, a channel protein, a membrane structural protein, a protein involved in adhesion, a protein involved in antigen presentation, or a protein involved in formation of high dimensional structure of a protein; recovering a budded baculovirus released from said host; and recovering the protein expressed from said budded baculovirus.

Thus, Applicants' invention includes that the protein is expressed in a budded baculovirus released from the host. In connection with this aspect of Applicants' invention, attention is directed to Applicants' specification, as filed, wherein in the "Background of the Invention" section appearing on pages 1 and 2, it is disclosed that:

> A baculovirus expression system enables high-level expression of a gene of interest by causing recombination of the gene in Sf9 cells using a promoter of a polyhedrin gene of baculovirus. A polyhedrin is expressed in the nucleus of Sf9 cell at a high level as an occlusion body which is a form to be used when viruses become latent within the cell. The baculovirus expression system where a recombinant protein is introduced into a polyhedrin gene and the expressed proteins are purified, has many advantages over that of *Escherichia coli*, such that the expressed proteins are hard to agglutinate and the expressed proteins undergo a posttranscriptional modification which is necessary for protein functions, such as addition of sugar chains and coordination of metal ion.
>
> Baculovirus has another life cycle. In order to proliferate and infect, baculovirus becomes a budded virus (Budded virus: this is also referred to as budded baculovirus in this specification), rupturing Sf9 cell membrane and being released outside the cell. Bouvier et al have reported that at this time a receptor of seven-transmembrane type recombined into the above polyhedrin protein is expressed on the cell membrane and recovered from the envelope of the budded baculovirus (Loisel TP, Ansanay H, St-Onge S, Gay B, Boulanger P, Strosberg AD, Marullo S, Bouvier M., Nat Biotechnol. 1997 Nov; 15(12): 1300-4., Recovery of homogeneous and functional beta 2-adrenergic receptors from extracellular baculovirus particles; and International Publication WO98/46777). It has also been reported that, whereas most receptors of seven-transmembrane type expressed in a host cell have a sugar chain structure which is not functional, only functional receptors are recovered from the viral envelope. However, Bouvier et al have not mentioned membrane proteins other than receptor proteins.

Thus, as can be seen from the discussion in Applicants' specification, there are two life cycles of baculovirus. In contrast to Bandman and Ikeda, the protein in the present invention is expressed in the budded baculovirus.

Each of Bandman and Ikeda do not teach or suggest that the protein is expressed in a budded baculovirus released from the host. While these documents may refer to the baculovirus expression system, the systems discussed in these documents is that which is disclosed in the above-noted "Background of the Invention" section in Applicants' specification. In the expression system of the present invention, the protein is expressed in a budded baculovirus released from the host. In contrast to the present invention, the protein in Bandman and Ikeda is expressed in host cell or culture solution.

Bandman discloses at column 1, in the paragraph appearing at lines 53-59 that retinol dehydrogenase is a membrane-bound enzyme, and at column 14, the paragraph appearing at lines 6-17, that a variety of expression vector/host systems may be utilized to contain and express sequences encoding HRoDH, including, at lines 11-12, "insect cell systems infected with virus expression vectors (e.g., baculovirus)". However, Bandman does not teach or suggest wherein the protein is expressed in the budded baculovirus. Moreover, Bandman may refer to expression in Sf90 cells, but does not refer to expression of the protein in a virus.

Ikeda discloses that a membrane protein which lacks membrane anchor domain is secreted in a supernatant of culture as a soluble protein. This is different from the expression system involved in the present invention wherein protein is expressed in a budded baculovirus released from the host. For example, in the present invention, a membrane protein can be embedded in a virus envelope and can be displayed on the virus. In Ikeda, the secreted protein is a soluble protein and is purified from the culture supernatant. Ikeda does not refer to the virus particles present in the culture supernatant. Further, the protein which is expressed in Ikeda is a mutant protein which lacks membrane anchor

domain. Such mutant protein is no longer membrane protein. In any event, as noted above, Ikeda does not teach or suggest that the protein is expressed in a budded baculovirus released from the host.

Thus, Applicants respectfully submit that the only teaching or suggestion that would lead one having ordinary skill in the art to arrive at Applicants' invention is within Applicants' disclosure, and the use of such disclosure by the Examiner is improper. In order to support the conclusion that the claimed invention is either anticipated or rendered obvious over the prior art, the prior art must either expressly or inherently teach the claimed invention or the Examiner must present a convincing line of reasoning why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references. Ex parte Clapp, 227 U.S.P.Q. 972 (B.O.A. 1985).

Additionally, each of the dependent claims is patentable over the prior art of record in view of the fact that each of these dependent claims includes the limitations of either independent claim 1 or 2. Moreover, each of the dependent claims is patentable over the prior art of record because the combination of features recited therein is not disclosed in the prior art of record, and it would not have been obvious to one having ordinary skill in the art to incorporate such dependent claim features into the invention as more broadly recited in independent claims 1 and 2.

In view of the above, the rejections of record are without appropriate basis, and should be withdrawn.

CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejection of record, and allow all the pending claims.

Allowance of the application is requested, with an early mailing of the Notices of Allowance and Allowability.

If the Examiner has any questions or wish to further discuss this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,
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APPENDIX

MARKED UP COPY OF AMENDED CLAIMS 1, 9 AND 12

1. (Amended) A method for expressing a protein selected from a membrane-bound enzyme, a substrate of the membrane-bound enzyme, a membrane-bound enzyme activator, a membrane-bound transport protein, a channel protein, a membrane structural protein, a protein involved in adhesion, a protein involved in antigen presentation, or a protein involved in formation of high dimensional structure of a protein by culturing a host infected with at least one [type of] recombinant baculovirus which contains a gene encoding said protein, wherein said protein is expressed in a budded baculovirus released from said host.

9. (Amended) A budded baculovirus which is released from a host infected with at least one [type of] baculovirus which contains a gene encoding a protein selected from a membrane-bound enzyme, a substrate of the membrane-bound enzyme, a membrane-bound enzyme activator, a membrane-bound transport protein, a channel protein, a membrane structural protein, a protein involved in adhesion, a protein involved in antigen presentation, or a protein involved in formation of high dimensional structure of a protein.

12. (Amended) A method for screening a chemical substance which activates or inhibits the function of two or more proteins selected from a membrane-bound enzyme, a substrate of the membrane-bound enzyme, a membrane-bound enzyme activator, a membrane-bound transport protein, a channel protein, a membrane structural protein, a protein involved in adhesion, a protein involved in antigen presentation, or a protein involved in formation of high dimensional structure of a protein, by co-infecting two or more different [types of] recombinant baculoviruses, each of

which contains a gene encoding a different [type] one of said [protein] two or more proteins; and co-expressing the function of said two or more proteins.

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MARKED UP COPY OF AMENDED ABSTRACT

ABSTRACT OF THE DISCLOSURE

[The purpose of the present invention is to provide a method] Method for efficiently expressing a protein in an active form by using baculovirus expression system wherein the protein is selected from a membrane-bound enzyme, a substrate of the membrane-bound enzyme, a membrane-bound enzyme activator, a membrane-bound transport protein, a channel protein, a membrane structural protein, a protein involved in adhesion, a protein involved in antigen presentation, or a protein involved in formation of high dimensional structure of a protein. [According to the present invention, there] There is provided a method for expressing such a protein [selected from a membrane-bound enzyme, a substrate of the membrane-bound enzyme, a membrane-bound enzyme activator, a membrane-bound transport protein, a channel protein, a membrane structural protein, a protein involved in adhesion, a protein involved in antigen presentation, or a protein involved in formation of high dimensional structure of a protein] by culturing a host infected with at least one type of recombinant baculovirus which contains a gene encoding [said] the protein, wherein [said] the protein is expressed in a budded baculovirus released from [said] the host.